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EXAMINER
FORMAN, BETTY J

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1634	25

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/440,829	Applicant(s) CHENCHIK ET AL.	
	Examiner BJ Forman	Art Unit 1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 July 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3 and 7-38* is/are pending in the application.

4a) Of the above claim(s) *24-34* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,7-23 and 35-38* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. This action is in response to papers filed 5 July 2002 in Paper No. 22 & 23 in which claims 2, 8, 15 and 36-38 were amended and a Supplemental Declaration under § 1.132 was submitted. All of the amendments have been thoroughly reviewed and entered. The previous rejection of Claims 2, 3, 15-17 under 35 U.S.C. 112, second paragraph in the Office Action of Paper No. 22 dated 8 January 2002 are withdrawn. The previous rejections under 35 U.S.C. 103 are maintained. All of the arguments have been thoroughly reviewed and are discussed below.

New grounds for rejection are discussed.

Currently claims 1-3, 7-23 and 35-38 are under prosecution.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 9 and 36-38 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a. Claim 9 is indefinite for the recitation "wherein said oligonucleotide probe is cross-linked to the surface of said support at at least two sites." because "sites" lacks proper antecedent basis in Claim 1 and therefore it is unclear whether the "at least two sites" are sites within a single probe (i.e. each single probe is cross-linked at least two times) or are sites on

the support (i.e. multiple copies of the probe are cross-linked to at least two sites on the support).

b. Claim 18 is indefinite for the recitation "said unique oligonucleotides" because "unique" lacks proper antecedent basis in Claim 14. It is suggested that Claim 18 be amended to provide proper antecedent basis e.g. replace "unique" with "long".

c. Claims 36-38 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential elements, such omission amounting to a gap between the elements. See MPEP § 2172.01. The omitted elements are: structural elements of the arrays which define or describe "hybridization efficiency"; which define or describe determining "variance in hybridization efficiency"; and which define or describe the structural elements that determine 10-fold variance.

d. Claims 36-38 are further indefinite for the recitation "using the hybridization efficiency assay described in the specification beginning at page 23, lines 4ff." because it is unclear what structural or compositional limitations are being described. It is suggested that the claims be amended to recite the missing structural elements which define or describe "hybridization efficiency", "variance in hybridization efficiency" and "10-fold" "variance".

Claim Rejections - 35 USC § 102

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) do not apply to the examination of this application as the application being examined was not (1) filed on or after November 29, 2000, or (2) voluntarily published under 35 U.S.C. 122(b). Therefore, this application is examined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

5. Claims 1-11, 14, 19 and 20 are rejected under 35 U.S.C. 102(e) as being anticipated by Ebersole et al (U.S. Patent No. 6,037,127, filed 26 November 1997).

Regarding Claim 1, Ebersole et al disclose an array comprising at least one pattern of probe oligonucleotide spots stably attached to the surface of a solid support wherein each probe spot comprises a probe composition made up of long oligonucleotide probes that range in length from about 50 to 100 nucleotides i.e. 45-57 (Example 7, Column 33, line 25-Column 34, line 52).

Regarding Claim 2, Ebersole et al disclose the array wherein two or more different target nucleic acids hybridize to different probe spots in said pattern (Column 33, lines 36-45).

Regarding Claim 3, Ebersole et al disclose the array wherein each probe spot in said pattern hybridizes to a different target nucleic acid (Column 33, lines 36-45).

Regarding Claim 7, Ebersole et al disclose the array wherein each of said long probes are covalently attached to said surface of said substrate (Column 33, lines 30-35).

Regarding Claim 8, Ebersole et al disclose the array wherein each of said long probes is crosslinked to the surface of said support (Column 33, lines 30-35).

Regarding Claim 9, Ebersole et al disclose the array wherein each of said probes is crosslinked to the surface at at least two sites e.g. probe p3 is crosslinked on Capture Zone 1, strips A through G (Column 33, lines 36-45 and Fig. 12).

Regarding Claim 10, Ebersole disclose the array wherein the spots on the array do not exceed a density of about 1000/cm^2 (Column 19, lines 38-55 and Fig 12).

Regarding Claim 11, Ebersole disclose the array wherein the spots on the array do not exceed a density of about 400/cm^2 (Column 19, lines 38-55 and Fig 12).

Regarding Claim 14, Ebersole et al disclose an array comprising at least one pattern of probe oligonucleotide spots stably attached to the surface of a solid support wherein each probe spot comprises a probe composition made up of long oligonucleotide probes that range in length from **about** 60 to 100 nucleotides i.e. 45-57 (Column 13, lines 21-26 and Example 7, Column 33, line 25-Column 34, line 52).

Regarding Claim 19, Ebersole disclose the array wherein the spots on the array do not exceed a density of about 1000/cm^2 (Column 19, lines 38-55 and Fig 12).

Regarding Claim 20, Ebersole disclose the array wherein the spots on the array do not exceed a density of about 400/cm^2 (Column 19, lines 38-55 and Fig 12).

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. Claims 12, 13, 15-18, 21, 22 and 36-37 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ebersole et al (U.S. Patent No. 6,037,127, filed 26 November 1997).

Regarding Claims 12 and 13, Ebersole et al teach the array comprising at least one pattern of probe oligonucleotide spots stably attached to the surface of a solid support wherein each probe spot comprises a probe composition made up of long oligonucleotide probes that

range in length from about 50 to 100 nucleotides (Example 7, Column 33, line 25-Column 34, line 52) wherein the number of spots is at least 21 (see Fig. 12) but they do not teach the number of spots range from about 50 to 50,000 (Claim 12) and from about 50 to 10,000 (Claim 13). However, the courts have stated that when a claimed device recites change in shape, size or dimension of a prior art device, the claimed device is not patentably distinct from the prior art device (531 F.2d at 1053, 189 USPQ at 148; In Gardner v. TEC Systems, Inc., 725 F.2d 1338, 220 USPQ 777 (Fed. Cir. 1984),cert. denied, 469 U.S. 830, 225 USPQ 232 (1984). Therefore, the claimed range of spots i.e. from about 50 to 50,000 (Claim 12) and from about 50 to 10,000 (Claim 13) is not patentably distinct from the array of Ebersole et al. Additionally, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the array comprising 21 spots of Ebersole et al. useful for detecting multiple analytes in a sample and to increase the number of spots to 50 to thereby include 50 known analyte-specific nucleic acids for the expected benefit of providing an array useful for detecting multiple clinically important analytes.

Regarding Claim 15, Ebersole et al teach the array wherein two or more different target nucleic acids hybridize to different probe spots in said pattern (Column 33, lines 36-45) but they do not teach the array comprises ten or more different probe spots each of which hybridize to a different target. However, the courts have stated that when a claimed device recites change in shape, size or dimension of a prior art device, the claimed device is not patentably distinct from the prior art device (531 F.2d at 1053, 189 USPQ at 148; In Gardner v. TEC Systems, Inc., 725 F.2d 1338, 220 USPQ 777 (Fed. Cir. 1984),cert. denied, 469 U.S. 830, 225 USPQ 232 (1984). Therefore, the claimed number of different spots i.e. ten or more is not patentably distinct from the array of Ebersole et al. Additionally, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the array comprising three different target-specific spots of Ebersole et al. useful for detecting multiple analytes in a sample and to increase the number of different spots to at least 10 to thereby

include 10 known analyte-specific nucleic acids for the expected benefit of providing an array useful for detecting multiple clinically important analytes.

Regarding Claim 16, Ebersole et al teach the array wherein each probe spot in said pattern hybridizes to a different target (Column 33, lines 36-45).

Regarding Claim 17, Ebersole et al teach the array wherein two or more spots in said pattern hybridize to the same target (Column 33, lines 36-45).

Regarding Claim 18, Ebersole et al teach the array wherein the oligonucleotide probes that range in length from about 60 to 90 nucleotides i.e. 47-57 (Example 7, Column 33, line 25-Column 34, line 52) and they teach the probes range in size from 10 to 300 (Column 13, lines 21-26) which clearly suggests the claimed range of from about 65-90. It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the probe length of Ebersole et al using routine experimentation based on the suggested probe lengths taught by Ebersole (i.e. 10 to 300; Column 13, lines 21-26) and to derive an optimal probe length (e.g. 65-90) for the expected benefits of maximizing probe function. It is noted that *In re Aller*, 220 F.2d 454,456, 105 USPQ 233,235 states where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum by routine experimentation.

Regarding Claims 21 and 22, Ebersole et al teach the array comprising at least one pattern of probe oligonucleotide spots stably attached to the surface of a solid support wherein each probe spot comprises a probe composition made up of long oligonucleotide probes that range in length from about 50 to 100 nucleotides (Example 7, Column 33, line 25-Column 34, line 52) wherein the number of spots is at least 21 (see Fig. 12) but they do not teach the number of spots range from about 50 to 50,000 (Claim 21) and from about 50 to 10,000 (Claim 22). However, the courts have stated that when a claimed device recites change in shape, size or dimension of a prior art device, the claimed device is not patentably distinct from the prior art device (531 F.2d at 1053, 189 USPQ at 148; In Gardner v. TEC Systems, Inc., 725 F.2d

1338, 220 USPQ 777 (Fed. Cir. 1984),cert. denied, 469 U.S. 830, 225 USPQ 232 (1984). Therefore, the claimed range of spots i.e. from about 50 to 50,000 (Claim 12) and from about 50 to 10,000 (Claim 13) is not patentably distinct from the array of Ebersole et al. Additionally, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the array comprising 21 spots of Ebersole et al. useful for detecting multiple analytes in a sample and to increase the number of spots to 50 to thereby include 50 known analyte-specific nucleic acids for the expected benefit of providing an array useful for detecting multiple clinically important analytes.

Regarding Claims 36 and 37, Ebersole et al. teach the arrays of Claims 1 and 14 wherein capture probes are designed and hybridization conditions adjusted using techniques known in the art to provide sensitive and specific detection of targets and optimize simultaneous detection of multiple targets (Column 21, lines 4-35) which clearly suggests the optimized conditions for simultaneous detecting of multiple targets clearly suggests the hybridization efficiency of the probes does not exceed 10-fold. However, the recitation "hybridization efficiency among any two probes...." does not limit the structure of the array because the recitation is functional language.

The courts have stated that claims drawn to an apparatus must be distinguished from the prior art in terms of structure rather than function see *In re Danly*, 263 F.2d 844, 847, 120 USPQ 528, 531 (CCPA1959). "[A]pparatus claims cover what a device is, not what a device does." Hewlett-Packard Co. v. Bausch & Lomb Inc., 909 F.2d 1464, 1469, 15 USPQ2d 1525,1528 (Fed. Cir. 1990) (see MPEP, 2114). Therefore, because "hybridization efficiency among any two probes...." does not define the array in terms of structure, the recitation does not further limit the array. Hence, Ebersole et al. teach the array as claimed.

8. Claims 23 and 38 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ebersole et al (U.S. Patent No. 6,037,127, filed 26 November 1997) in view of Van Ness et al. (U.S. Patent No. 5,667,976, issued 16 September 1997).

Regarding Claim 23, Ebersole et al disclose an array comprising at least one pattern of probe oligonucleotide spots of a density that does not exceed about 400/cm^2 covalently attached to the surface of a solid support wherein each probe spot comprises a probe composition made up of long oligonucleotide probes that range in length from about 60 to 90 nucleotides i.e. 45-57 (Example 7, Column 33, line 25-Column 34, line 52) and they teach the probes range in size from 10 to 300 (Column 13, lines 21-26) which clearly suggests the claimed range of from about 65-90. It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the probe length of Ebersole et al using routine experimentation based on the suggested probe lengths taught by Ebersole (i.e. 10 to 300; Column 13, lines 21-26) and to derive an optimal probe length (e.g. 65-90) for the expected benefits of maximizing probe function. It is noted that *In re Aller*, 220 F.2d 454,456, 105 USPQ 233,235 states where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum by routine experimentation. Ebersole et al do not teach the probes are attached to a glass surface. However, probes attached to a glass surface was well known in the art at the time the claimed invention was made a taught by Van Ness et al. Specifically, Van Ness et al. teach an array comprising a pattern of probe oligonucleotide spots attached the surface of a solid support (i.e. two to ten capture oligonucleotide-coated beads, Column 10, lines 24-26) wherein the spots on the array do not exceed a density of about 400/cm^2 i.e. the preferred bead diameter is .09 inch (0.23 cm) therefore, the beads on the array cannot exceed a density of 400/cm^2 (Column 3, lines 53-59) wherein said probes are covalently attached to said surface of said substrate (Column 3 lines 53-59) wherein said probes are covalently bound to said surface of said solid support (Column 10, lines 24-30) and wherein a

preferred solid support is glass (Column 4, lines 1-7 and Claim 2). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the glass surface of Van Ness et al. to the solid support of Ebersole et al. because Van Ness et al. teach glass is a preferred solid support for attachment of nucleic acids (Column 11, lines 54-67). Therefore, one of skill in the art would have been motivated to modify the solid support of Ebersole et al. with the preferred glass support as taught by Van Ness et al. for the expected benefit of preferred oligonucleotide attachment as taught by Van Ness et al. (Column 11, lines 54-58).

Regarding Claim 38, Ebersole et al. teach the array of Claim 23 wherein capture probes are designed and hybridization conditions adjusted using techniques known in the art to provide sensitive and specific detection of targets and optimize simultaneous detection of multiple targets (Column 21, lines 4-35) which clearly suggests the optimized conditions for simultaneous detecting of multiple targets clearly suggests the hybridization efficiency of the probes does not exceed 10-fold. However, the recitation "hybridization efficiency among any two probes...." does not limit the structure of the array because the recitation is functional language.

The courts have stated that claims drawn to an apparatus must be distinguished from the prior art in terms of structure rather than function see *In re Danly*, 263 F.2d 844, 847, 120 USPQ 528, 531 (CCPA1959). "[A]pparatus claims cover what a device is, not what a device does." Hewlett-Packard Co. v. Bausch & Lomb Inc., 909 F.2d 1464, 1469, 15 USPQ2d 1525,1528 (Fed. Cir. 1990) (see MPEP, 2114). Therefore, because "hybridization efficiency among any two probes...." does not define the array in terms of structure, the recitation does not further limit the array. Hence, Ebersole et al. teach the array as claimed.

9. Claim 35 is rejected under 35 U.S.C. 103(a) as being unpatentable over Ebersole et al (U.S. Patent No. 6,037,127, filed 26 November 1997) in view of Stratagene (catalog, 1988. page 39).

Regarding Claim 35, Ebersole et al teach an array comprising at least one pattern of probe oligonucleotide spots stably attached to the surface of a solid support wherein each probe spot comprises a probe composition made up of long oligonucleotide probes that range in length from about 50 to 100 nucleotides i.e. 45-57 (Example 7, Column 33, line 25-Column 34, line 52) but they do not teach the array in a kit. Stratagene catalog teaches a motivation to combine reagents into kit format (page 39). It would have been obvious to one having ordinary skill in the art at the time the invention was made to combine the array of Ebersole et al into a kit format as discussed by Stratagene catalog since the Stratagene catalog teaches a motivation for combining reagents of use in an assay into a kit, "Each kit provides two services: 1) a variety of different reagents have been assembled and pre-mixed specifically for a defined set of experiments. 2) The other service provided in a kit is quality control" (page 39, column 1).

10. Claims 1-3, 7, 8, 10-22 and 35-37 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sheiness et al. (U.S. Patent No. 5,776,694, issued 7 July 1998).

Regarding Claim 1, Sheiness et al. teach an array (i.e. dipstick) comprising a pattern of probe oligonucleotide spots stably associated with the surface of a solid support (i.e. at least two capture oligonucleotide-coated beads, Column 7, lines 50-61) wherein each probe spot of said pattern comprises a probe composition made up of probes that range in length from about 50 to 100 nucleotides (i.e. the capture oligonucleotides range from about 6 to about 150 bases,

Column 14, lines 19-28). The courts have stated that in the case where the claimed ranges "overlap or lie inside ranges disclosed by the prior art" a prima facie case of obviousness exists.

> In re Geisler, 116 F.3d 1465, 1469-71, 43 USPQ2d 1362, 1365-66 (Fed. Cir. 1997) (Claim reciting thickness of a protective layer as falling within a range of "50 to 100 Angstroms" considered prima facie obvious in view of prior art reference teaching that "for suitable protection, the thickness of the protective layer should be not less than about 10 nm [i.e., 100 Angstroms]." The court stated that "by stating that suitable protection' is provided if the protective layer is about' 100 Angstroms thick, [the prior art reference] directly teaches the use of a thickness within [applicant's] claimed range.") (see MPEP 2144.05 I).

Additionally, the courts have stated that where the general conditions are known in the art "it is not inventive to discover the optimal or workable ranges by routine experimentation" (*In re Aller*, 220 F.2d 454,456, 105 USPQ 233,235).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the probes of about 6 to 150 nucleotides in the array of Sheiness et al. and using routine experimentation derive probes within the range taught by Sheiness et al. (e.g. 50 to 100 nucleotides) to thereby provide the optimal range of nucleotide probe length for the expected benefit of optimizing array components and maximizing array function.

Regarding Claim 2, Sheiness et al. teach the array wherein two or more different target nucleic acids are represented in said pattern i.e. a first bead selectively hybridizes to a prokaryotic nucleic acid target and a second bead selectively hybridizes to a eukaryotic nucleic acid target, Column 7, lines 55-61).

Regarding Claim 3, Sheiness et al. teach the array wherein each probe spot hybridizes to a different target nucleic acid (Column 18, lines 52-56).

Regarding Claim 7, Sheiness et al. teach the array wherein said probes are covalently attached to said surface of said substrate (Column 18 lines 52-55).

Regarding Claim 8, Sheiness et al. teach the array wherein each of said probes is crosslinked to the surface of said support at at least one site i.e. via cyanuric chloride (Column 17, lines 30-65).

Regarding Claim 10, Sheiness et al. teach the array wherein the spots on the array do not exceed a density of about 1000/cm^2 i.e. the preferred bead diameter is .09 inch (0.23 cm) therefore, the beads on the array cannot exceed a density of 1000/cm^2 (Column 16, lines 50-57).

Regarding Claim 11, Sheiness et al. teach the array wherein the spots on the array do not exceed a density of about 400/cm^2 i.e. the preferred bead diameter is .09 inch (0.23 cm) therefore, the beads on the array cannot exceed a density of 400/cm^2 (Column 16, lines 50-57).

Regarding Claims 12 and 13, Sheiness et al. teach the array comprises from about two to about ten spots (i.e. beads) but they do not teach the number of spot range from about 50 to 50,000 (Claim 12) and from about 50 to 10,000 (Claim 13). However, the courts have stated that when a claimed device recites change in shape, size or dimension of a prior art device, the claimed device is not patentably distinct from the prior art device (531 F.2d at 1053, 189 USPQ at 148; In Gardner v. TEC Systems, Inc., 725 F.2d 1338, 220 USPQ 777 (Fed. Cir. 1984), cert. denied, 469 U.S. 830, 225 USPQ 232 (1984). Therefore, the claimed range of spots i.e. from about 50 to 50,000 (Claim 12) and from about 50 to 10,000 (Claim 13) is not patentably distinct from the array of Sheiness et al. Additionally, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the array comprising 10 spots of Sheiness et al. useful for detecting pathogenic target nucleic acids in a sample (Abstract) and to increase the number of spots to 50 to thereby include 50 known pathogen-specific nucleic acids (Column 43-44) for the expected benefit of providing an array useful for detecting multiple clinically important microbes.

Regarding Claim 14, Sheiness et al. teach an array (i.e. dipstick) comprising a pattern of probe oligonucleotide spots attached the surface of a solid support (i.e. at least two capture

oligonucleotide-coated beads, Column 7, lines 50-61) wherein each probe spot of said pattern comprises a probe composition made up of probes that range in length from about 60 to 100 nucleotides (i.e. the capture oligonucleotides range from about 6 to about 150 bases, Column 14, lines 19-28) and wherein said probes are covalently bound to said surface of said solid support (Column 18, lines 52-55). The courts have stated that in the case where the claimed ranges "overlap or lie inside ranges disclosed by the prior art" a prima facie case of obviousness exists. Additionally, the courts have stated that where the general conditions are known in the art "it is not inventive to discover the optimal or workable ranges by routine experimentation" (*In re Aller*, 220 F.2d 454,456, 105 USPQ 233,235). Therefore, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the probes of about 6 to 150 nucleotides in the array of Sheiness et al. and using routine experimentation derive probes within the range taught by Sheiness et al. (e.g. 60 to 100 nucleotides) to thereby provide the optimal range of nucleotide probe length for the expected benefit of optimizing array components and maximizing array function.

Regarding Claim 15, Sheiness et al. teach the array wherein ten different target nucleic acids are represented i.e. the dipstick comprises 10 beads and each bead has different capture probes attached (Column 18, lines 46-56).

Regarding Claim 16, Sheiness et al. teach the array wherein each probe spot hybridizes to a different target nucleic acid (Column 18, lines 52-56).

Regarding Claim 17, Sheiness et al. teach the array wherein two probe spots hybridize to the same target i.e. UP553 hybridizes to the complement of UP 053 (Example 8, Column 45, lines 45-55)

Regarding Claim 18, Sheiness et al. teach the array wherein each oligonucleotide ranges from about 65-90 nucleotides (i.e. the capture oligonucleotides range from about 6 to about 150 bases, Column 14, lines 19-28) and wherein said probes are covalently bound to said surface of said solid support (Column 17, lines 30-34). The courts have stated that in the case

where the claimed ranges "overlap or lie inside ranges disclosed by the prior art" a prima facie case of obviousness exists. Therefore, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the probes of about 6 to 150 nucleotides in the array of Sheiness et al. and using routine experimentation derive probes within the range taught by Sheiness et al. (e.g. 65 to 90 nucleotides) to thereby provide the optimal range of nucleotide probe length for the expected benefit of optimizing array components and maximizing array function.

Regarding Claim 19, Sheiness et al. teach the array wherein the spots on the array do not exceed a density of about 1000/cm^2 i.e. the preferred bead diameter is .09 inch (0.23 cm) therefore, the beads on the array cannot exceed a density of 1000/cm^2 (Column 16, lines50-57).

Regarding Claim 20, Sheiness et al. teach the array wherein the spots on the array do not exceed a density of about 400/cm^2 i.e. the preferred bead diameter is .09 inch (0.23 cm) therefore, the beads on the array cannot exceed a density of 400/cm^2 (Column 16, lines 50-57).

Regarding Claims 21 and 22, Sheiness et al. teach the array comprises from about two to about ten spots (i.e. beads) but they do not teach the number of spot range from about 50 to 50,000 (Claim 12) and from about 50 to 10,000 (Claim 13). However, the courts have stated that when a claimed device recites change in shape, size or dimension of a prior art device, the claimed device is not patentably distinct from the prior art device (531 F.2d at 1053, 189 USPQ at 148; In Gardner v. TEC Systems, Inc., 725 F.2d 1338, 220 USPQ 777 (Fed. Cir. 1984), cert. denied, 469 U.S. 830, 225 USPQ 232 (1984). Therefore, the claimed range of spots i.e. from about 50 to 50,000 (Claim 12) and from about 50 to 10,000 (Claim 13) is not patentably distinct from the array of Sheiness et al. Additionally, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the array comprising 10 spots of Sheiness et al. useful for detecting pathogenic target nucleic acids in a sample (Abstract) and to increase the number of spots to 50 to thereby include 50 known

pathogen-specific nucleic acids (Column 43-44) for the expected benefit of providing an array useful for detecting multiple clinically important microbes.

Regarding Claim 35, Sheiness et al. teach a kit comprising the array of Claim 1 (Column 7, lines 48-65).

Regarding Claims 36 and 37, Sheiness et al. teach the arrays of Claims 1 and 14 wherein capture probes are designed and hybridization conditions adjusted using techniques known in the art to provide sensitive and specific detection of targets and optimize simultaneous detection of multiple targets (Column 14, lines 51-65) which clearly suggests the optimized conditions for simultaneous detecting of multiple targets clearly suggests the hybridization efficiency of the probes does not exceed 10-fold. However, the recitation "hybridization efficiency among any two probes...." does not limit the structure of the array because the recitation is functional language.

The courts have stated that claims drawn to an apparatus must be distinguished from the prior art in terms of structure rather than function see *In re Danly*, 263 F.2d 844, 847, 120 USPQ 528, 531 (CCPA1959). "[A]pparatus claims cover what a device is, not what a device does." Hewlett-Packard Co. v. Bausch & Lomb Inc., 909 F.2d 1464, 1469, 15 USPQ2d 1525,1528 (Fed. Cir. 1990) (see MPEP, 2114). Therefore, because "hybridization efficiency among any two probes...." does not define the array in terms of structure, the recitation does not further limit the array. Hence, Sheiness et al. teach the array as claimed.

11. Claim 9 is rejected under 35 U.S.C. 103(a) as being unpatentable over Sheiness et al. (U.S. Patent No. 5,776,694, issued 7 July 1998) in view of Graves, D. (Tibtech, 1999, 17: 127-134).

Regarding Claim 9, Sheiness et al. teach an array (i.e. dipstick) comprising a pattern of probe oligonucleotide spots stably associated with the surface of a solid support (i.e. at least two capture oligonucleotide-coated beads, Column 7, lines 50-61) wherein each probe spot of said pattern comprises a probe composition made up of probes that range in length from about 50 to 100 nucleotides (i.e. the capture oligonucleotides range from about 6 to about 150 bases, Column 14, lines 19-28) wherein said probes are covalently attached to said surface of said substrate (Column 18 lines 52-55) but they do not teach each probe is cross-linked to the surface at at least two sites. However, multiple cross-linked probes were well known in the art at the time the claimed invention was made as taught by Graves. Specifically, Graves teaches that multiple cross-links hold probes firmly in place and improves hybridization signal (page 131, right column, third paragraph, lines 3-8 and page 132, left column, lines 6-23). Therefore, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the crosslinking teaching of Graves to the oligonucleotide probe attachment of Sheiness et al. and to crosslink the probes at at least two sites to thereby hold the probes firmly in place for the expected benefit of improving hybridization signal detection as taught by Graves (page 132, left column, lines 6-23).

12. Claims 23 and 38 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sheiness et al. (U.S. Patent No. 5,776,694, issued 7 July 1998) in view of Van Ness et al. (U.S. Patent No. 5,667,976, issued 16 September 1997).

Regarding Claim 23, Sheiness et al. teach an array (i.e. dipstick) comprising a pattern of probe oligonucleotide spots attached the surface of a solid support (i.e. at least two capture oligonucleotide-coated beads, Column 7, lines 50-61) wherein the spots on the array do not exceed a density of about 400/cm^2 i.e. the preferred bead diameter is .09 inch (0.23 cm)

therefore, the beads on the array cannot exceed a density of 400/cm^2, wherein said probes are covalently attached to said surface of said substrate (Column 18 lines 52-55) wherein each probe spot of said pattern comprises a probe composition made up of probes that range in length from about 65 to 90 nucleotides (i.e. the capture oligonucleotides range from about 6 to about 150 bases, Column 14, lines 19-28) and wherein said probes are covalently bound to said surface of said solid support (Column 17, lines 30-34). Sheiness et al. teach the array wherein the probes are covalently attached to beads and wherein the beads are comprised of any material to which a nucleic acid can be immobilized (Column 16, lines 38-44) but they do not specifically teach the bead is comprised of glass. However, glass beads on arrays (i.e. dipsticks) were well known in the art at the time the claimed invention was made a taught by Van Ness et al. Specifically, Van Ness et al. teach an array (i.e. dipstick) comprising a pattern of probe oligonucleotide spots attached the surface of a solid support (i.e. two to ten capture oligonucleotide-coated beads, Column 10, lines 24-26) wherein the spots on the array do not exceed a density of about 400/cm^2 i.e. the preferred bead diameter is .09 inch (0.23 cm) therefore, the beads on the array cannot exceed a density of 400/cm^2 (Column 3, lines 53-59) wherein said probes are covalently attached to said surface of said substrate (Column 3 lines 53-59) wherein said probes are covalently bound to said surface of said solid support (Column 10, lines 24-30) and wherein a preferred solid support is glass (Column 4, lines 1-7 and Claim 2). Additionally, Van Ness et al. teach glass beads permit high density oligonucleotide attachment (Column 11, lines 54-67). Therefore, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the glass bead teaching of Van Ness et al. to the solid support of Sheiness et al. who teach any solid support onto which oligonucleotides are attached because Van Ness et al. teach glass is a preferred solid support for high density attachment of nucleic acids (Column 11, lines 54-67). Therefore, one of skill in the art would have been motivated to modify the bead solid support of Sheiness et al. with the preferred glass bead as taught by Van Ness et al. for the expected benefit of high

density oligonucleotide attachment as taught by Van Ness et al. (Column 11, lines 54-58). Sheiness et al. teach a range of probe length which overlaps the claimed range of 65-90 nucleotides (i.e. the capture oligonucleotides range from about 6 to about 150 bases, Column 14, lines 19-28). The courts have stated that in the case where the claimed ranges "overlap or lie inside ranges disclosed by the prior art" a prima facie case of obviousness exists. Additionally, the courts have stated that where the general conditions are known in the art "it is not inventive to discover the optimal or workable ranges by routine experimentation" (*In re Aller*, 220 F.2d 454,456, 105 USPQ 233,235). Therefore, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the probes of about 6 to 150 nucleotides in the array of Sheiness et al. and using routine experimentation derive probes within the range taught by Sheiness et al. (e.g. 65 to 90 nucleotides) to thereby provide the optimal range of nucleotide probe length for the expected benefit of optimizing array components and maximizing array function.

Regarding Claim 38, Sheiness et al. teach the array of Claim 23 wherein capture probes are designed and hybridization conditions adjusted using techniques known in the art to provide sensitive and specific detection of targets and optimize simultaneous detection of multiple targets (Column 14, lines 51-65) which clearly suggests the optimized conditions for simultaneous detecting of multiple targets clearly suggests the hybridization efficiency of the probes does not exceed 10-fold. However, the recitation "hybridization efficiency among any two probes...." does not limit the structure of the array because the recitation is functional language.

The courts have stated that claims drawn to an apparatus must be distinguished from the prior art in terms of structure rather than function see *In re Danly*, 263 F.2d 844, 847, 120 USPQ 528, 531 (CCPA1959). "[A]pparatus claims cover what a device is, not what a device does." Hewlett-Packard Co. v. Bausch & Lomb Inc., 909 F.2d 1464, 1469, 15 USPQ2d 1525,1528 (Fed. Cir. 1990) (see MPEP, 2114). Therefore, because "hybridization efficiency

among any two probes...." does not define the array in terms of structure, the recitation does not further limit the array. Hence, Sheiness et al. teach the array as claimed.

Response to Arguments

13. Applicant argues that the claimed narrow range of probe length provides unexpected results. Applicant further states that because the claimed narrow range provides unexpected results and because the claimed narrow range is not suggested by Sheiness who teach a broader range of probe length, the instantly claimed arrays are not obvious over Sheiness. The arguments have been considered but are not found persuasive for the reasons stated below i.e. arguments regarding unexpected results are not found persuasive because the declaration of Dr. Chenchik does not provide adequate evidence of unexpected results for the claimed invention.

Response to Declaration

14. The Declaration filed on 5 July 2002 under 37 CFR 1.132 has been considered but is ineffective to overcome the Sheiness et al. or Ebersole et al reference. The Declaration of Dr. Chenchik is not found persuasive for several reasons. First, Dr. Chenchik states that Examples1-5 in the specification demonstrate unexpected results for the invention as claimed. However, Examples 1-5 merely illustrate hybridization signals derived **exclusively** from radio-isotopically labeled 50nt, 60nt, 70nt, 80nt, 90nt and 100nt probes (and specifically, the probes listed on table 1) immobilized on amynoproply-glass. The claims are drawn to a much broader array comprising probe spots ranging in length from about 50 to 100 which encompasses probes which comprising various labels and unlabeled probes and encompasses a very large genus of supports. Therefore, results obtained from Examples 1-5 are not results obtained

from the claimed invention. As such, Examples 1-5 do not illustrate that the claimed invention provides unexpected results. Second, Dr. Chenchik discusses the hybridization results obtained from probes of 35nt, 50nt, 60nt, 70nt, 80nt, 90nt and 100nt and states that hybridization efficiency depends on the size of the immobilized probe in the range between 35 and 100 nucleotides. Dr. Chenchik does not compare the hybridization efficiency of the claimed about 50 to 100 nucleotides to probes longer and or shorter which would clearly demonstrate that the claimed range provides results unexpected over the range taught by the Sheiness et al. or Ebersole et al. Third, Dr. Chenchik does not address sequence composition of the probes and their respective melting/hybridization temperatures. Because hybridization efficiently is dependent upon Tm, and because the claims encompass probes of a very large range of Tm, the declaration does not demonstrate unexpected results for the invention as claimed. Finally, Dr. Chenchik states that the unexpected finding is that the hybridization rate "dramatically depends on the size of immobilized probe in the range between 50 and 100 nucleotides."(page 6, last paragraph). However, the fact that hybridization rate depends on size within the claimed range (.e. hybridization between 50 mer and 60, 80, 100 mer is about 3, 4 and 5 fold higher respectively) does not demonstrate that the claimed range provides unexpected results over the ranges taught by Sheiness et al. or Ebersole et al but merely illustrates hybridization within the claimed range for isotopically labeled probes immobilized on amynomopoly-glass. As such, the declaration of Dr. Chenchik is not sufficient to over come the teachings of Sheiness et al. or Ebersole et al.

Conclusion

15. No claim is allowed.

16. The examiner's Art Unit has changed from 1655 to 1634. Please address future correspondence to Art Unit 1634.

17. Any inquiry concerning this communication or earlier communications from the examiner should be directed to BJ Forman whose telephone number is (703) 306-5878. The examiner can normally be reached on 6:30 TO 4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones can be reached on (703) 308-1152. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-8724 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

BJ Forman, Ph.D.
Patent Examiner
Art Unit: 1634
October 10, 2002